IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application
Inventor(s): Parry Guilford et al.
SC/Serial No.: 10/565,068
Confirm. No.: 3673
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Title: MARKERS FOR DETECTION OF GASTRIC CANCER

PATENT APPLICATION

Art Unit: 1643
Examiner: Alana Harris

Customer No. 66936

REPLY TO FINAL OFFICE ACTION

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This REPLY is filed with a Request for Continued Examination ("RCE"), and is in response to the final Office Action mailed on 18 March, 2010. A Petition for a Extension of Time for three (3) months is filed herewith, including the required Small Entity fees. Applicants also have included an IDS.

Amendments

Please amend the above-identified application as follows:

In the Claims:

Please amend claims 1, 2, 9-12, 19-21, 25, 26, and 28-30. Please cancel claims 8 and 27.

1. (Currently amended) A method for detecting gastric cancer, comprising:

(a) providing a ~~biological~~ sample of blood; and

(b) detecting over-expression of a cystatin SN ("CST1") protein ~~or cystatin SN peptide~~ having the sequence of SEQ ID NO:108 in said blood sample.

2. (Currently amended) The method of claim 1, further comprising detecting over-expression of [[a]] at least one additional GTM family member protein selected from the group consisting of matrix metalloproteinase 12 (MMP12), inhibin ("INHBA"), insulin-like growth factor 7 ("IGFBP7"), gamma-glutamyl hydrolase ("GGH"), leucine proline-enriched proteoglycan ("LEPRE1"), cystatin S ("CST4"), secreted frizzled-related protein 4 ("SFRP4"), asporin ("ASPN"), cell growth regulator with EF hand domain 1 ("CGREF1"), kallikrein, tissue inhibitor of metalloproteinase 1 ("TIMP1"), secreted acidic cysteine-rich protein ("SPARC"), transforming growth factor ("TGFB1"), EGF-containing fibulin-like extracellular matrix protein 2 ("EFEMP2"), lumican ("LUM"), stannin ("SNN"), secreted phosphoprotein 1 ("SPP1"), chondroitin sulfate proteoglycan 2 ("CSPG2"), carboxypeptidase N ("CPN2"), N-acylsphingosine amidohydrolase ("ASAH1"), serine protease 11 ("PRSS11"), secreted frizzled-related protein 2 ("SFRP2"), phospholipase A2, group XIIB ("PLA2G12B"), spondin 2 ("SPON2") , extracellular matrix protein ("SPON2"), olfactomedin 1 ("OLFM1"), thrombospondin repeat containing 1 ("TSRC1"), thrombospondin 2 ("THBS2"), adlican, cystatin SA ("CST2"), lysyl oxidase-like enzyme 2 ("LOXL2"), thyroglobulin ("TG"), transforming growth factor beta1 ("TGFB1"), transforming growth factor β induced protein ("TGFB-I"), serine or cysteine proteinase inhibitor clade H ("SERPINH1"), serine or cysteine proteinase inhibitor clade B ("SERPINB5"), matrix metalloproteinase 2 ("MMP2"), proprotein convertase subtilisin/kexin type 5 ("PCSK5"), kallikrein 10 ("KLK10"), hyaluronin and proteoglycan link protein 4 ("HAPLN4"), serine protease 11 ("PRSS11"), and transmembrane 6 superfamily member 2 ("TM6SF2").

3. (Withdrawn) The method of claim 2, wherein said step of detecting is carried out by detecting over-expression of GTM mRNA.

4. (Withdrawn) The method of claim 2, wherein said step of detecting is carried out by detecting over-expression of GMT cDNA.

5. (Withdrawn) The method of claim 4, wherein said step of detecting is carried out using an oligonucleotide complementary to at least a portion of said GMT cDNA.

6. (Withdrawn) The method of claim 4, wherein said step of detecting is carried out using qPCR method using a forward primer and a reverse primer.

7. (Canceled)

8. (Canceled)

9. (Currently amended) The method of claim [[8]] 1, ~~wherein~~ said step of detecting [[is]] being carried out using an antibody directed against said CST1 ~~cystatin SN~~ protein ~~peptide~~.

10. (Currently amended) The method of claim 9, ~~wherein~~ said step of detecting [[is]] being carried out using a sandwich-type immunoassay method.

11. (Currently amended) The method of claim 9, ~~wherein~~ said antibody [[is]] being a monoclonal antibody.

12. (Currently amended) The method of claim 9, ~~wherein~~ said antibody [[is]] being a polyclonal antiserum.

13. (Withdrawn) A device for detecting a GTM, comprising:

a substrate having a GTM capture reagent thereon; and

a detector associated with said substrate, said detector capable of detecting a GTM associated with said capture reagent.

14. (Withdrawn) The device of claim 13, wherein said GTM capture reagent is an oligonucleotide.

15. (Withdrawn) The device of claim 13, wherein said GTM capture reagent is an antibody.

16. (Withdrawn) A kit for detecting cancer, comprising:

a substrate having a GTM capture reagent thereon;

a means for visualizing a complex of said GMT capture agent and a GMT;

reagents; and

instructions for use.

17. (Withdrawn) The kit of claim 16, wherein said GTM capture reagent is a GTM-specific oligonucleotide.

18. (Withdrawn) The kit of claim 16, wherein said GTM capture reagent is a GTM-specific antibody selective for a GTM-oligonucleotide, a GTM protein or a GTM peptide.

19. (Currently amended) A method for detecting gastric cancer, comprising the steps of:

providing a [[test]] blood sample from a patient suspected of having gastric cancer;

measuring the presence in said blood sample of a cystatin SN protein ~~or a cystatin SN peptide~~ having the sequence of SEQ ID NO:108 ~~in said test sample~~; and

comparing the amount of said cystatin SN protein ~~or peptide~~ present in said [[test]] blood sample with a threshold value that distinguishes a normal cystatin SN protein levels from a cancer-indicative level ~~obtained from a sample from a subject not having~~ gastric cancer.

20. (Currently amended) A method for screening for gastric cancer, comprising the steps of:

providing a [[test]] blood sample from a test subject;

measuring the presence in said blood sample of a cystatin SN protein ~~or cystatin SN peptide~~ having the sequence of SEQ ID NO:108 ~~in said test sample~~; and

comparing the amount of said cystatin SN protein ~~or cystatin SN peptide~~ present [[is]] in said [[test]] blood sample with a value obtained from a control sample from a subject not having gastric cancer, and

finding over-expression of said cystatin SN protein ~~or cystatin SN peptide~~ in said [[test]]] blood sample compared to said control sample when the presence of said cystatin SN protein meets or exceeds a threshold value over the control sample.

21. (Currently amended) The method of claim 19, further comprising detecting over-expression of [[a]] at least one additional GTM family member protein selected from the group consisting of MMP12, INHBA, IGFBP7, GGH, LEPRE1, CST4, SFRP4, ASPN, CGREF1, KLK10, TIMP1, SPARC, TGFB1, EFEMP2,

LUM, SNN, SPP1, CSPG2, ASAH1, PRSS11, SFRP2, PLA2G12B, SPON2, OLFM1, TSRC1, THBS2, adlican, CST2, LOXL2, TG, TGFB1, SERPINH1, SERPINB5, MMP2, PCSK5 and TM6SF2.

22. (Withdrawn) The method of claim 19, wherein said GTM is an oligonucleotide specific for a GTM.

23. (Withdrawn) The method of claim 22, wherein said oligonucleotide is DNA.

24. (Withdrawn) The method of claim 22, wherein said oligonucleotide is RNA.

25. (Currently amended) The method of claim 19, ~~wherein~~ said step of measuring [[uses]] using an ELISA assay.

26. (Currently amended) The method of claim 19, ~~wherein~~ said test sample [[is]] being obtained from plasma.

27. (Canceled) The method of claim 19, wherein said test sample is obtained from tissue, urine, gastric fluid, serum or stool.

28. (Currently amended) The method of claim 1, further comprising measuring over-expression of SERPINH1 or SERPINB5 in said blood sample.

29. (Currently amended) The method of claim 1, further comprising measuring over-expression of one or more of SFRP4, SFRP2, TSRC1, THBS2, LOXL2, SERPINH1, SERPINB5, and CGR11 in said blood sample.

30. (Currently amended) The method of claim 1, further comprising measuring over-expression of one or more proteins selected from the group consisting of adlican, ASPN, CSPG2, cystatin SA ("CST2"), cystatin S ("CST4"), EFEMP2, GGH, INHBA, IGFBP7, LKL10, LEPRE1, LUM, LOXL2, MMP12, TIMP1, ASAH1, SPP1, SFRP2, SFRP4, CGR11, THBS2, SPARC, PRSS11, TG, and TGFBI in said blood sample.

Remarks

The above Amendments and these Remarks are in REPLY to the Final Office Action mailed 18 March, 2010, and are filed with an RCE and with an IDS.

Claims 3-6, 13-18 and 22-24 were withdrawn in a prior REPLY in response to a restriction requirement, and Claim 7 was cancelled in the previous REPLY to the Office Action mailed on 12 November 2008. In this Amendment, filed with together with an RCE, Claims 8 and 27 are cancelled, and Claims 1, 2, 9-12, 19-21, 25, 26, and 28-30 remain pending and are currently amended.

Included with this REPLY are: (1) an RCE; (2) a Petition for Extension of Time for three (3) months for a Small Entity; and (3) the appropriate Small Entity fees for the Petition for Extension of Time, and the RCE, with authorization to deduct the Small Entity fees from Deposit Account 50-4089.

Claim Rejections Under 35 U.S.C. § 112 ¶ 2

The Examiner rejected Claims 1, 2, 8-12, 19-21, 25-30 "as indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." In particular, the Examiner indicated that "it is not clear if SEQ ID: 108 is assigned or designated as the cystatin SN (CST1) protein or the CST1 peptide." Office Action ("OA") at 4.

Applicants have amended the claims to disclose "cystatin SN (CST1) protein." Applicants submit that the amendment addresses the Examiner's Rejection and the claims as amended now comply with §112 ¶2. Accordingly, Applicants respectfully request reconsideration of the Examiner's §112 ¶2 rejection.

Claim Rejections Under 35 U.S.C. §102

Claims 1, 2, 8-12, 19-21, 25-27, and 30 stand rejected under 35 U.S.C. §102(e) as anticipated by US 2004/0232350 (the "Afar Reference").

Applicants have canceled claims 8 and 27. Applicants have amended the independent claims in a manner that obviates the Examiner's rejections based on the Afar Reference. In particular, the Afar Reference does not disclose and enable detecting CST1 protein in a blood sample.

Independent Claim 1 as amended discloses "A method for detecting gastric cancer, comprising: . . . detecting over-expression of a . . . []CST1[] protein having the sequence of SEQ ID NO:108 in said blood sample." Applicants have made similar amendments to independent Claims 19 and 20. Applicants respectfully submit that the amendments render moot the Examiner's rejection under §102. Applicants respectfully request reconsideration of the rejections and allowance of the claims.

Claim Rejections Under 35 U.S.C. §103

Claims 1, 2, 8-12, 19-21 and 25-30 stand rejected under 35 U.S.C. §103(a) as obvious over the Afar Reference, in view of Mack *et al.*, US 2004/0076955 (the "Mack Reference") and Clarke *et al.*, US 2006/0019256 (the "Clarke Reference").

Applicants have amended the claims and believe that the amendments render moot the Examiner's rejection under §103. Applicants respectfully request reconsideration of the rejection and allowance of the claims.

Conclusions

Applicants respectfully submit that the rejections under 35 U.S.C. §112 ¶2, and 35 U.S.C. §§102 and 103 are overcome. Applicants request the Examiner to reconsider the rejections and to allow the claims.

A Petition for Extension of Time of three (3) months, an RCE, and the required Small Entity fees are included herewith.

The Examiner is respectfully requested to telephone the undersigned if he can assist in any way in expediting issuance of a patent. The Commissioner is authorized to deduct from or refund funds to Deposit Account 50-4089 for any additional fee related to this Reply.

Respectfully submitted,

Date: September 17, 2010

By: 

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